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by O. S. Shramchenko

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PROXIMATE RESULTS IN THE THERAPY OF SKIN CANCER WITH OMAINE OINTMENT(1)

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From the Rostov-on-Don Scientific Research Institute of Roentgenology, Radiology and Oncology (Director, P. N. Snegirev) of the Ministry of Health RSFSR

In 1950 G. P. Men'shikov, V. V. Kiselev and A. A. Beer isolated a new alkaloid -- desacetylcolchicine, which was designated colchamine or omaine. Ye. M. Vermel' who had tested it on animals came to the conclusion that omaine is 10 to 14 times less toxic than colchicine, while the destructive effect of its action on tumor cells is several times higher.

Starting in 1956, at Rostov Institute of Roentgenology, Radiology and Oncology, 0.5 percent of omaine ointment was used on 46 patients (15 men and 31 women) in the ambulatory treatment of skin cancer.

Basically, patients in the first (44), second (one patient) and third (one patient) stages of the disease were subjected to treatment, and nine of them received radiation therapy prior to this.

(1) From the Editorial Office. The method of therapy of skin cancer with omaine ointment does not replace the method of radiation therapy of this form of tumor, and there is no reason to use omaine (colchamine) therapy in all cases of skin cancer, especially because the remote results of omaine therapy are still insufficiently studied. It is also necessary to take into consideration that in the official instructions omaine ointment is called the colchamine ointment.

The tumors in these patients were localized on the face skin (with the exception of one case where the tumor developed in the region of the neck).

Prior to treatment, a histological examination of tumor tissue was made. Basal cell carcinoma was found in 28 patients, squamous cell carcinoma -- in 13, chronic inflammation in one patient, and in four patients only isolated areas of tissue proliferation were detected.

After taking a specimen from the focus of the lesion for a biopsy, a thorough hemostasis was performed and omaine ointment (about one gram) was immediately applied, including no less than one cm of the healthy surface around the tumor. Treatment was conducted daily (one female patient received treatment every other day).

In some patients melting of the tissue took place after only two to three applications; the necrotic areas became separated, the ulcer cleared up and its margins became soft. Such a course was particularly observable in patients having the exophytic form of cancer. In endophytic forms the separation of necrotic tissue took place after five or six applications. During this period, there developed in the surrounding healthy tissues hyperemia, pain, edema; fibrinous films appeared not only on the healthy tissue but on the neoplastic ones as well. If these reactive manifestations became more pronounced, the treatment was interrupted for one to three days, and the entire area was covered with a streptomycin or penicillin emulsion with anaesthesine until the inflammatory changes abated, after which the omaine ointment therapy was resumed. On the whole, no less than 10 applications of the ointment were required until the clinical manifestations of the tumor disappeared and the bottom of the ulcer became covered with granulations.

During the process of treatment, a control speciment of tissue was taken from seven patients for histologic examination. In one patient, after seven applications, young granulation tissue was detected; in another case, after 11 applications, markedly changed tumor masses were detected; in one female patient, after 13 applications, together with a pronounced mesodermal reaction, there remained predominant elements of squamous cell carcinoma; the same was observed in another female patient after 30 applications of the ointment. In three cases, after 10 to 12 treatments with omaine ointment, no signs of a tumor were detected.

In these cases, three to four days following termination of the course of therapy, a small crust appeared on the surface of the ulcer, under which epithelization was taking place. The healing was completed, on the average, within 10 to 12 days. In one female patient the epithelization was

completed on the 10th day. The control biopsy showed the presence of granulation tissue. The patient is alive, and no relapse has occurred up to the present time.

To eliminate clinical symptoms of cancer, it was necessary to carry out, on the average, 13 to 14 applications of omaine ointment. In no patient did the tumor disappear in fewer than 10 applications, and in one case one could speak of a clinical recovery only after 42 applications.

Following the recovery there remains a fine, smooth scar surrounded by pigmentation.

One of the instances of a successful use of omaine ointment is the treatment of female patient O., 62 years of age, who had been admitted on 2 April 1957 with complaints of a nonhealing ulcer of the skin of the upper lip on the right side. The ulcer first appeared in 1937. At first, the patient contacted physicians in the city of Gor'kiy where coagulation was attained. The ulcer healed, but a year later it reappeared and commenced to grow gradually. In 1946, 1948 and 1950 a course of X-ray therapy was given; the ulcer did not heal, though it stopped growing. In 1953 the ulcer began to grow again, in connection with which an intra-tissue implantation of radium needles (3,697 and 5,000 gamma/roentgen) was performed in 1955 and 1956. However, the ulcer did not disappear, and only a temporary improvement took place. When the patient was admitted to the Institute, her general condition was satisfactory. There was on the skin of the upper lip, on the right side, an ulcer three to four cm in size with indurated spindle-like edges and covered with a crust in the center. The tumor grew through almost the entire thickness of the soft labial tissues, but the mucosa was movable (see Fig. a). The clinical diagnosis was skin cancer of the upper lip third stage. Histological diagnosis: basal cellular carcinoma.

The tumor proved to be resistant to omaine treatment; following 30 applications of the ointment, there were detected in the control specimen squamous carcinoma elements with some focal development of granulation tissue, among which were also seen isolated groups of tumor cells. The treatment was continued for a total of 42 applications. The patient was discharged. A check-up examination three months later showed at the seat of the ulcer a smooth scar indurated in the region of the margin of the upper lip, with dry crusts at the naso-labial fold (see Fib. b). The patient is still in good health. She stated that, after 20 years, the omaine treatment made it possible for her for the first time to remove the bandage from her face.

One of the important advantages of omaine ointment is

a b

the possibility of its utilization in areas where under the thin layer of skin a cartilage is present which is very sensitive to radiation effects. Therefore, for instance, cancer situated in the region of the cochlea would ordinarily require surgical treatment which leaves cosmetic defects. The employment of omaine ointment for the treatment of such localization of skin cancer leads to smooth recovery, without necrosis of the cartilagenous lamina ever having been observed. Apparently, this is due to the basic properties of omaine which specifically destroys only blastomatous tissue.

As was previously mentioned, nine men with relapses had been subjected to omaine ointment therapy; in four of them the carcinomatous ulcer would reappear persistently despite various therapeutic procedures: excision (simple and with an electrotome), X-ray therapy, the use of radium (intra-tissue and via application). As an example, may serve thecited excerpt from the history chart.

In all nine cases smooth healing took place under the effect of omaine. Subsequent observations showed no recurrence in any of these patients.

According to the data of the literature (I. T. Kramorenko, Ye. M. Vermel', A. Kh. Movsesyan), there

were no complications during the treatment with 0.5 percent omaine ointment in the first and second stage of skin cancer. We, nevertheless, had some complications of local as well as general character which, however, quickly disappeared following the end of treatment. Thus, in female patient D., 70 years of age, a first stage skin cancer of the left cheek was found. After an eight-day treatment the patient lost consciousness and her temperature rose to 37.5°C. The bandage with omaine ointment was immediately removed and the treatment was interrupted for two days. The treatment was completed after 14 applications. A fine, soft scar surrounded by pigmentation remained at the seat of ulceration.

It is necessary to note that the rise in temperature to 37.3° - 37.5°C observed in a number of patients apparently had been due to the reaction of the organism to the local inflammatory focus.

Skin irritations were observed in a few cases. Thus, in two patients there appeared around the ointment-treated skin surface a dermatitis of from five to six cm in width. These manifestations disappeared after the termination of treatment. In one case the skin reaction was manifested over the entire body.

In patient G., 59 years of age, there appeared a dermatitis of the trunk, face, and upper and lower extremities following six applications of omaine ointment to the skin of the right temporal region for a basal cell carcinoma. The omaine therapy was suspended for two days and was resumed following the disappearance of the rash. A total of 14 applications was made. Complete recovery. A fine scar remained at the seat of the ulcer after the end of the treatment. The skin around the scar was pigmented.

The dermatitis required almost no treatment, the sole condition being a temporary suspension of omaine ointment application. Subsequent use of the ointment caused no recurrence of dermatitis in any of these cases, and the treatment in all of them was carried out to the end. Of other complications, there was observed in three patients an edema of the cheek and lower eyelid which also quickly disappeared following a short suspension of treatment.

Two patients showed general weakness, apparently due to intoxication. A blood transfusion was found necessary, though no change in the blood formula had been observed in any of these patients. In general, examination of the peripheral blood manifested no significant changes in the hemopoietic organs of these patients and no leukopenia, in particular, was observed.

Of 46 patients treated with omaine ointment for skin cancer the recurrence of the tumor appeared in 13 percent.

Ye. M. Vermel' and I. T. Kramorenko observed relapses in 10 percent, A. Kh. Movsesyan -- in 7.6 percent, I. T. Kramorenko -- in 20 percent. Our data correspond to the results obtained by Ye. M. Vermel'.

In our patients there was observed a very early and repeated relapse following omaine therapy.

Patient F., 34 years of age. Diagnosis: Basal cell carcinoma of the skin of the left temporal region, first stage. Following 12 applications the ulcer healed, leaving a soft scar. One month later, the patient returned with a recurrence of the tumor, which was confirmed by histological analysis. Repeated treatment with omaine ointment (18 applications). Patient discharged as cured. At the seat of cancer -- a smooth scar. One month later -- another relapse. An electrical excision was performed. Histological findings: basocellular carcinoma.

Among the peculiarities of the clinical course of cancer in this case we must mention the protracted character of the process (12 months prior to the start of treatment), as well as unsuccessful repeated "cauterizations" carried out by dermatologists.

In two patients the relapse occurred four months after the end of treatment, in one case -- after six months, in one case -- after a year, and in the last case -- after a year and five months. In four patients the relapse thus occurred within the first six months, a fact which indicates in these instances that the cancer process had not been completed after omaine therapy. Histological examination of tissue following the end of treatment is difficult to achieve in all patients, and, besides, it does not always provide the correct answer. Therefore, the basic criterion of the success of conducted therapeutic measures still remains a dynamic observation of the patient during remote periods following the termination of treatment.

We possess the observations as of 1 January 1959 of all 46 patients with clinical manifestations of skin cancer who had been treated with omaine (of these, 41 with a diagnosis confirmed histologically). As has already been mentioned relapses at various periods occurred in six patients. Forty patients are healthy (period observation from 14 to 24 months on 23 individuals, and from 24 to 34 months -- on 17 individuals).

Conclusions

1. Omaine ointment selectively affects the tumor cells, and scarcely involves the healthy tissues (inflammatory reaction).

2. Treatment of skin cancer with omaine brings satisfactory, direct, and rapid results.

3. Since the method is available for wide use, omaine ointment can be recommended in the practice of therapeutic establishments of the general type, including the district hospitals.

4. In contrast to other methods of treatment, omaine ointment may be effectively employed in patients with relapses following other methods of treatment of skin cancer.

5. Omaine ointment can be recommended in such cases where radiation therapy is connected with complications, as for instance, in the treatment of skin cancer of the cochlea.

6. During the omaine ointment therapy certain complications are possible which, upon their early diagnosis, can be eliminated following a two-to-three-day suspension of treatment.

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